

## PEER REVIEW HISTORY

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## ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Prevalence of long-term health conditions in adults with autism - observational study of a whole country population
<b>AUTHORS</b>	Rydzewska, Ewelina; Hughes-McCormack, Laura; Gillberg, Christopher; Henderson, Angela; MacIntyre, Cecilia; Rintoul, Julie; Cooper, Sally-Ann

## VERSION 1 – REVIEW

<b>REVIEWER</b>	Elspeth Bradley Associate Professor, University of Toronto, Canada
<b>REVIEW RETURNED</b>	30-Jan-2018

<b>GENERAL COMMENTS</b>	<p>This is indeed a unique study of co morbidity in adults with autism with an impressive high response rate in a whole country population. The methods are rigorous, results well-presented and the style of communication made the article a pleasure to read. Tables provide a wealth of information and are clearly laid out.</p> <p>The main limitation (namely that the information on autism, intellectual disabilities (ID) and health status is from “broad-brush” census data rather than from detailed questions to clarify the categories being studied) is outside the researchers control. This limitation is identified and appropriately discussed in the Strengths and Limitations Section.</p> <p>About a third of the Discussion (the last paragraph) is focused on ID and females with autism. From my perspective it was difficult to follow the logic of the authors explanations throughout this last part (lines 12 – 19 page 10). For example, the evidence the authors point to in their findings from this study, did not to my mind support the statements they were making e.g.,</p> <p>“A view has been expressed that autism is currently underdiagnosed in more intellectually-able females compared with males.<sup>13</sup> Our findings provide some evidence to support this view, given that 34% of women and only 27% of men with autism reported accompanying intellectual disabilities.” How does 34% of woman reporting ID support autism being underdiagnosed in more intellectually able females compared to males?</p> <p>Curiously, at least as far as I could determine, there was no discussion about the finding of an autism prevalence rate of 0.2% in this whole country population of adults. This is very low compared to Brugha et al rate of almost 1% in an English population. Some explanation would be of interest to the reader and the wider research community. Could this 0.2% represent a “biased” group within those individuals with autism so identified – or is there reason to consider that the prevalence of autism is lower in Scotland compared to England? Does the answer to this have implications for</p>
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	<p>understanding the male / female autism prevalence ratios found in this Scottish population?</p> <p>Readers may also be curious to know why the researchers did not include in their reported study a breakdown of autism and intellectual disabilities and comparison of OR for hearing, vision, mental health conditions, physical disability and other condition, between autism with and autism without ID. This specific information would also be helpful in raising awareness of co morbidities and in planning services (e.g., LD services). Perhaps this is to be reported elsewhere? Does this analysis offer a greater understanding of the profile of the 0.2% of the Scottish population identified with autism and does this autism ID and non-ID profile match findings from other studies e.g., higher health comorbidities in autism ID?</p>
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<b>REVIEWER</b>	<p>Lisa Croen Division of Research, Kaiser Permanente Northern California, USA</p>
<b>REVIEW RETURNED</b>	17-Feb-2018

<b>GENERAL COMMENTS</b>	<p>This study describes prevalence of 6 self- or proxy-reported health conditions among adults 25+ in Scotland, comparing the rates of conditions between those who reported having autism and those who did not. The large, country-wide study population is a strength. However, there are numerous methodologic shortcomings limiting the interpretability of the results. Most importantly, the results are based on self-report of broad categories of conditions. Autism is assumed from an affirmative answer to the questions regarding 'developmental disorder', since the only examples given for this category were autism and Asperger's. This is a huge assumption and no data are presented regarding the validity of these data.</p> <p>Specific comments follow:</p> <p>Abstract: The last sentence "Autism may be underdiagnosed in women" is not supported by what is presented in the results section of the abstract.</p> <p>Introduction: This statement about the Croen paper is somewhat inaccurate. It should read "only those individuals who had received healthcare at Kaiser Permanente Northern California were identified". Everybody was in the study, regardless of if they received healthcare for a particular condition.</p> <p>Croen study included hearing impairment/deafness and vision impairment/blindness, but statement in introduction ignores this fact. "Neither of these two studies included a general population comparison group. We were unable to identify any other studies on these conditions in adults with autism."</p> <p>Methods:</p> <p>Census achieved 94% response rate. Any information on the 6% left out? Likely that adults with disabilities, communication impairments, health conditions were over-represented. Need to comment on this in discussion as a limitation of study. Data were imputed for these 6% but not clear how well this imputation matches actual characteristics of those left out.</p> <p>All data on autism and health conditions were self-reported. Any data on validity of these self-reports? Other condition and no condition combined into 'other condition' category. Thus, data on 'other condition' is meaningless. Everybody answering yes to developmental disability considered to have autism – also very big</p>
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	<p>assumption which may seriously overcount autism.</p> <p>Results: Be careful with language used. Replace 'had autism' with 'reported autism' since it is not known whether individuals actually had the condition they were reporting.</p> <p>Age and sex analyses only done within the autism group. Why is that? Patterns of risk by age and sex may be similar in the non-autistic population, so autism-specific results are not that informative. A more informative analysis strategy would be to look at ORs for each health condition stratified by age and sex.</p> <p>Discussion: Incomplete review of previous literature. For example, Croen study does report on hearing and vision impairments recorded in medical records, but this is not mentioned in the discussion section. What conditions are captured in 'physical disability' category? This is a broad, ill-defined category, and not very informative. Other studies report on specific health conditions (cardiovascular, immune, neurologic, etc).</p> <p>Last paragraph of discussion regarding rate of autism diagnosis in women and what findings mean with regard to severity of autism is going way beyond the data.</p> <p>Study did not systematically assess 'health needs' as stated in Strengths paragraph of discussion.</p> <p>Table 1 – would be more informative to show column percentages rather than row percentages, so reader could easily compare age distributions between autism and non-autism groups.</p> <p>Tables 3 and 4: replace with Age- and</p>
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## VERSION 1 – AUTHOR RESPONSE

### Reviewers' Comments to Author:

#### Reviewer: 1

This is indeed a unique study of co morbidity in adults with autism with an impressive high response rate in a whole country population. The methods are rigorous, results well-presented and the style of communication made the article a pleasure to read. Tables provide a wealth of information and are clearly laid out. The main limitation (namely that the information on autism, intellectual disabilities (ID) and health status is from "broad-brush" census data rather than from detailed questions to clarify the categories being studied) is outside the researchers control. This limitation is identified and appropriately discussed in the Strengths and Limitations Section.

1. About a third of the Discussion (the last paragraph) is focused on ID and females with autism. From my perspective it was difficult to follow the logic of the authors explanations throughout this last part (lines 12 – 19 page 10). For example, the evidence the authors point to in their findings from this study, did not to my mind support the statements they were making e.g., "A view has been expressed that autism is currently underdiagnosed in more intellectually-able females compared with males.<sup>13</sup> Our findings provide some evidence to support this view, given that 34% of women and only 27% of men with autism reported accompanying intellectual disabilities." How does 34% of woman reporting ID support autism being underdiagnosed in more intellectually able females compared to males?

Response: We have carefully revised the paragraph to improve clarity, as follows: “A view has been expressed that autism is currently underdiagnosed in more intellectually-able females compared with males.<sup>13</sup> We found that 34% of women compared with only 27% of men with autism reported accompanying intellectual disabilities, so the female population with autism was intellectually less able than the male population with autism. Our findings therefore provide some evidence to support the view of under-diagnosis of autism in the more intellectually-able women. Many conditions are related to intellectual level, with there being a gradient across the whole spread of intelligence (not just intellectual disabilities).<sup>14</sup> If autism is underdiagnosed in more intellectually-able women, one therefore might expect more comorbidities to be found in women than men” (page 10-11).

2. Curiously, at least as far as I could determine, there was no discussion about the finding of an autism prevalence rate of 0.2% in this whole country population of adults. This is very low compared to Brugha et al rate of almost 1% in an English population. Some explanation would be of interest to the reader and the wider research community. Could this 0.2% represent a “biased” group within those individuals with autism so identified – or is there reason to consider that the prevalence of autism is lower in Scotland compared to England? Does the answer to this have implications for understanding the male/female autism prevalence ratios found in this Scottish population?

Response: We have expanded our discussion on this in the strengths and limitations section, to address the point made by the reviewer: “.....the concept of autistic spectrum disorder has broadened in recent years; our findings relate to the narrower definition that was used to diagnose autism in the past, as the study is one of adults who most likely were originally diagnosed in childhood. This accounts for the 0.2% identified prevalence; more recent studies conducting autism assessments have reported higher prevalence.<sup>16</sup>” (page 11).

3. Readers may also be curious to know why the researchers did not include in their reported study a breakdown of autism and intellectual disabilities and comparison of OR for hearing, vision, mental health conditions, physical disability and other condition, between autism with and autism without ID. This specific information would also be helpful in raising awareness of co morbidities and in planning services (e.g., LD services). Perhaps this is to be reported elsewhere? Does this analysis offer a greater understanding of the profile of the 0.2% of the Scottish population identified with autism and does this autism ID and non-ID profile match findings from other studies e.g., higher health comorbidities in autism ID?

Response: The paper already includes 4 data-dense tables as well as the text. We have previously published data on comorbidities in the population with intellectual disabilities, and so now focus this study on adults with autism. Comorbidities were indeed higher in those with intellectual disabilities than autism.

Reviewer: 2

This study describes prevalence of 6 self- or proxy-reported health conditions among adults 25+ in Scotland, comparing the rates of conditions between those who reported having autism and those who did not. The large, country-wide study population is a strength. However, there are numerous methodologic shortcomings limiting the interpretability of the results. Most importantly, the results are based on self-report of broad categories of conditions. Autism is assumed from an affirmative answer to the questions regarding ‘developmental disorder’, since the only examples given for this category were autism and Asperger’s. This is a huge assumption and no data are presented regarding the validity of these data. Specific comments follow:

1. Abstract: The last sentence “Autism may be underdiagnosed in women” is not supported by what is presented in the results section of the abstract.

Response: We have expanded the results section of the abstract: Contrary to findings within the general population, female gender predicted all conditions within the population with reported autism, “including intellectual disabilities (OR=1.4)” (page 2). This adds support to the conclusion that “Autism may be underdiagnosed in more able women” (page 2-3).

2. Introduction: This statement about the Croen paper is somewhat inaccurate. It should read “only those individuals who had received healthcare at Kaiser Permanente Northern California were identified”. Everybody was in the study, regardless of if they received healthcare for a particular condition.

Response: We have corrected this text to: “only those individuals with an existing record of autism in their medical records were identified as having autism” (page 4).

3. Croen study included hearing impairment/deafness and vision impairment/blindness, but statement in introduction ignores this fact. “Neither of these two studies included a general population comparison group. We were unable to identify any other studies on these conditions in adults with autism.”

Response: We have corrected this error, by adding: “One exception is the North California study of a wide range of conditions recorded in medical records which found 16 (1.1%) of adults with autism to have low vision or blindness (OR=7.85), and 71 (4.7%) with hearing impairment (OR=2.35).9” (page 5).

4. Methods: Census achieved 94% response rate. Any information on the 6% left out? Likely that adults with disabilities, communication impairments, health conditions were over-represented. Need to comment on this in discussion as a limitation of study. Data were imputed for these 6% but not clear how well this imputation matches actual characteristics of those left out.

Response: A detailed imputation method was used, and we have added the following further detail on this process: “The edit and imputation methodology used by the Census team was adapted from the Office for National Statistics rigorous and systematic guidelines:

<http://webarchive.nationalarchives.gov.uk/20160108193745/http://www.ons.gov.uk/ons/guide-method/method-quality/survey-methodology-bulletin/smb-69/index.html> Further details on how the Census population estimates were arrived at are available at:

<http://www.scotlandscensus.gov.uk/documents/censusresults/release1b/re11bmethodology.pdf>

Full details of the methodology and other background information on Scotland’s Census 2011 are available at: <http://www.scotlandscensus.gov.uk/supporting-information> (page 6).

Additionally, we have added the following to the limitations section: “Finally, whilst we describe the imputation process, we cannot state with certainty whether or not the imputed 6% of records contained the same, more or fewer proportion of adults with autism, but note that this missing 6% is a small proportion overall” (page 12).

5. All data on autism and health conditions were self-reported. Any data on validity of these self-reports? Other condition and no condition combined into ‘other condition’ category. Thus, data on ‘other condition’ is meaningless. Everybody answering yes to developmental disability considered to have autism – also very big assumption which may seriously overcount autism.

Response: We have expanded the section ‘Strengths/Limitations’ on discussion of reporting: “Respondents reported whether or not each person was known to have autism rather than each person having an assessment for autism, so some reporting error is possible” (page 11).

“Long-term illness, disease or condition” and “other condition” were merged into a single category (not “other conditions” and “no condition”). We have rewritten this to improve clarity on this point: “Following internal requirements for all Scotland’s Census 2011 outputs stipulated by the National Records of Scotland, options 8 (long-term illness, disease or condition) and 9 (other condition) were merged and coded as one category of ‘other condition’; thus, this term is used henceforth when referring to both these categories” (page 7).

We discuss the use of the term developmental disorder in the ‘strengths/limitations’ section of the discussion. The wording of this question was planned in detail by the Census team, at the request of autistic people in Scotland: “Limitations include the use of the term ‘developmental disorders’ in the Census, although the clarification of this term provided on the Census form included only autistic spectrum disorder and Asperger’s syndrome. Furthermore, the developmental disorders category was specifically distinguished from intellectual disabilities, dyslexia, and mental health conditions. Hence, we consider that respondents will have replied accordingly, i.e. responded regarding autism. However, we have no means to check this” (page 11).

6. Results: Be careful with language used. Replace ‘had autism’ with ‘reported autism’ since it is not known whether individuals actually had the condition they were reporting.

Response: We have made this amendment throughout.

7. Age and sex analyses only done within the autism group. Why is that? Patterns of risk by age and sex may be similar in the non-autistic population, so autism-specific results are not that informative. A more informative analysis strategy would be to look at ORs for each health condition stratified by age and sex.

Response: Table 3 reports ORs with age and gender and autism all included in the regressions as potential independent predictors of each of the condition for the whole population. Table 4 reports for just within the autism population. These tables show that the age and gender patterns are different for the autism population.

8. Discussion: Incomplete review of previous literature. For example, Croen study does report on hearing and vision impairments recorded in medical records, but this is not mentioned in the discussion section. What conditions are captured in ‘physical disability’ category? This is a broad, ill-defined category, and not very informative. Other studies report on specific health conditions (cardiovascular, immune, neurologic, etc).

Response: We have improved this by adding the hearing and vision data from Croen’s study and drawing comparisons: “We found 14% with hearing impairment (range 7%-46% depending on age group; 5%-44% for men and 11%-47% for women), and 12% with visual impairments (range 7%-30% depending on age group; 7%-27% for men and 10%-35% for women), notably higher than the rates recorded in medical records reported in the North California study (4.7% and 1.1% respectively, though ORs were not dissimilar),9 likely reflecting the different study methodologies” (page 10).

Physical disability is indeed a functional state, not one specific condition. It is similar in this respect to autism, and to intellectual disability. We do not think this means these terms are not very informative. We do not think that conditions that are described as “cardiovascular”, “immune” nor “neurologic” (as in the Croen study) are any more specific, as they encompass a multitude of different conditions, and they convey no information on functional impact. These are just different ways of presenting information; both approaches are informative.

9. Last paragraph of discussion regarding rate of autism diagnosis in women and what findings mean with regard to severity of autism is going way beyond the data.

Response: We have improved this discussion with rewriting (see response to reviewer 1) (page 11). Additionally, we have rewritten the implications accordingly: “Women with reported autism had a higher rate of intellectual disabilities than men which possibly suggests that more-able women may be less likely to be diagnosed than men; hence require improved care and support” (page 12).

10. Study did not systematically assess ‘health needs’ as stated in Strengths paragraph of discussion.

Response: We have amended ‘health needs’ to ‘selected long-term conditions’: “systematic enquiry of everyone regarding autism and selected long-term conditions” (page 11). We do not claim to have undertaken assessments.

11. Table 1 – would be more informative to show column percentages rather than row percentages, so reader could easily compare age distributions between autism and non-autism groups.

Response: We are keen in Table 1 to show the prevalence of autism in the whole population by age and gender, so do not wish to amend Table 1. We will follow the editor’s advice regarding adding an additional table or amending the table.

12. Tables 3 and 4: replace with Age- and sex- stratified analyses.

Response: Please see our response to point 7 – we believe the regression analyses as they are presented are informative. We could add the interaction term age x autism to Table 3, but will follow the editor’s advice on this.

## VERSION 2 – REVIEW

<b>REVIEWER</b>	Elspeth Bradley University of Toronto, Canada
<b>REVIEW RETURNED</b>	05-Apr-2018

<b>GENERAL COMMENTS</b>	<p>Thank you for your responses to Reviewer One Comments #1-3.</p> <p>Re: Authors response to Reviewer One, Comment #1 This is in regards to the text: “A view has been expressed that autism is currently underdiagnosed in more intellectually-able females compared with males. We found that 34% of women compared with only 27% of men with autism reported accompanying intellectual disabilities, so the female population with autism was intellectually less able than the male population with autism. Our findings therefore provide some evidence to support the view of under-diagnosis of autism in the more intellectually-able women.”</p> <p>Reviewer One: I am still unable to follow the logic of the interpretation “Our findings therefore provide some evidence to support the view of under-diagnosis of autism in the more intellectually-able women?” Has this something to do with an underling assumption that the female autism population and the male autism population are the same intellectually? If so is there any</p>
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	<p>clinical evidence for this? Or perhaps to do with the nature of self/proxy reporting and the likelihood that there was proxy (rather than self) reporting for intellectually disabled individuals? Or perhaps to do with whether the interpretation of the result relates to the total population of males with autism and the total population of females with autism or referring only to the population of males with ID and the population with females with ID – or referring to “the more intellectually-able women” within in the population of females with autism and intellectual disability? I wonder if the authors could clarify their logic and assumptions in coming to the conclusion “Our findings therefore provide some evidence to support the view of under-diagnosis of autism in the more intellectually-able women?”.</p> <p>Re: Authors response to Reviewer One, Comment #2 Reviewer One: Thank you for drawing readers attention to this in the strengths and limitations section.</p> <p>Re: Authors response to Reviewer One, Comment #3 Reviewer One: I anticipate many readers would be interested in these related studies (autism in this data set with and without reported intellectual disabilities) and comparison of OR for the variables studied between autism with and without intellectual disabilities. Perhaps this reference(s) could be provided?</p>
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## VERSION 2 – AUTHOR RESPONSE

### Response to editorial comments:

#### **bmjopen-2018-021792.R1: Prevalence of long-term health conditions in adults with autism - observational study of a whole country population**

Reviewer 2 did not agree to review your revision, so we assessed your responses to the reviewer's comments in-house. Unfortunately, while reviewer 1 was supportive, we did not feel that you adequately addressed some of reviewer 2's most serious concerns in this revised submission. We have provided some further feedback towards the end of this letter.

**\*\*\*Response:** Reviewer 1 is a recognised expert on this topic and we are therefore grateful for her time in reviewing the manuscript twice, her advice, and appreciate her support for the revision. We have addressed reviewer 2's comments further as outlined below.

1. Your rebuttal letter did not provide any reassurances about the validity of the reporting of autism diagnoses from this data source, although we appreciate this has been acknowledged as a limitation. Are there any published studies that have examined the extent of this reporting error using the same or similar data sources? Were you not able to carry out assessments/ use alternative methods to verify autism diagnoses, at least for a subset of your sample? Unfortunately, this reduced the confidence that we had in the soundness of the conclusions drawn from the data presented.

**\*\*\*Response:** The data is from a national survey. Considerable detail went into developing the survey and ensuring its accuracy, and we have added more detail on this with a new paragraph in the methods, rather than just referring to the overarching methodological source documents, as follows (pages 7-8):

“As part of the methodological preparations for Scotland's Census, 2011, the General Register Office for Scotland commissioned Ipsos MORI Scotland to undertake cognitive question testing of question 20 on long term health conditions and disabilities. The aim was primarily to test whether the questions were answered accurately and willingly by respondents, and what changes might be required to improve data quality and/or the acceptability of the response options. Cognitive interviewing is a



widely used approach to critically evaluate survey questionnaires.<sup>13</sup> It enables researchers to modify survey material to enhance clarity. Retrospective probing was deemed to be the most appropriate of the different techniques for the Census. The questions were tested with 102 participants with a mix of gender and age, both with and without the health conditions and disabilities (including people with more than one of the conditions), to ensure accurate and willing completion, and included people with autism, intellectual disabilities, dyslexia, dyspraxia, speech impairment, mental health conditions (both milder and more serious), and other long-term conditions. This resulted in a redesign of the question on autism to “Developmental disorder, for example autism spectrum disorder or Asperger’s syndrome” in order to accurately capture specifically the data on autism. The questions on the other conditions tested (some of which, from a medical perspective, can be considered as developmental disorders) did not require any modification. Further information can be found at: <http://www.scotlandscensus.gov.uk/documents/research/2011-census-health-disability-questions.pdf> <http://www.scotlandscensus.gov.uk/documents/legislation/changes-to-gov-statement-report.pdf>

Additionally, we wish to highlight to the editor that autism is a life-long condition which impacts continually on daily functioning. It is not a remitting-relapsing disorder, nor one that can have onset later in life, nor which may resolve. Autistic people live with their disabilities on a daily basis, as do their family members if they live with them. Given the acceptability of the revised question to autistic people, it is not likely to have been overlooked nor misunderstood on completion, nor autism forgotten about given the daily challenges the condition presents.

2. We also did not feel that you adequately addressed reviewer 2’s concern about the assumption that all people reporting a diagnosis of developmental disorder have autism. According to the methods section, the census asks respondents if they have developmental disorder with autistic spectrum disorder or Asperger’s syndrome given as examples. You have not presented any evidence to show that the vast majority of respondents are referring to autistic spectrum disorder or Asperger’s syndrome as opposed to another developmental disorder. Unless there is a way of verifying that the respondents included in your sample have an autism diagnosis then we do not feel that you are providing reliable conclusions about autistic people from the data presented.

**\*\*\*Response:** We have provided the additional information described above to editorial point 1, which explains that the question was carefully worded like this specifically to capture autism data (page 7-8).

3. We were also concerned that the conclusions are going beyond the data presented in places. We agree with reviewer 1’s comment below regarding your conclusion about the under-diagnosis of autism in more intellectually-able women. As you are not examining under diagnoses in intellectually-able men and women in this study we do not see how it is possible to make this inference.

**\*\*\*Response:** We were happy to tone this down (it is not at all the main thrust of the paper – indeed we would be happy to delete this paragraph altogether if the editor so advises), by:

- Deleting this following comment from the conclusion of the abstract, so that this interpretation is not mentioned in the abstract (page 2-3): ~~“Autism may be underdiagnosed in more able women.”~~
- Amending the discussion, by qualifying the interpretation of our own results through addition of the word “may”, and by adding an additional sentence to the end of this paragraph on this interpretation (page 11): “A view has been expressed that autism is currently underdiagnosed in more intellectually-able females compared with males.<sup>14</sup> We found that 34% of women compared with only 27% of men with autism reported accompanying intellectual disabilities, so the female population with autism was intellectually less able than the male population with autism. Our findings may therefore provide some evidence to support the view of under-diagnosis of autism in the more intellectually-able women. Alternatively, women and men with autism may actually be intellectually different.”
- Amending the interpretation: “If autism is underdiagnosed in more intellectually-able women....”, to the factual statement: “Given the lower average intelligence we found in the autistic women than the autistic men....”, when discussing rates of the other conditions they had (page 11): “Many conditions are related to intellectual level, with there being a gradient across the whole spread of intelligence (not just intellectual disabilities).<sup>16</sup> ~~If autism is underdiagnosed in more intellectually-able women,~~ Given the lower average intelligence we found in the autistic women than the autistic men, one might expect more comorbidities to be found in the women than the men.”

- Removing the following sentence from the implications for clinicians section (page 13): “~~Women with reported autism had a higher rate of intellectual disabilities than men which possibly suggests that more-able women may be less likely to be diagnosed than men, hence require improved care and support.~~”

Reviewer's Comments to Author:

Reviewer: 1

Reviewer Name: Elspeth Bradley

Institution and Country: University of Toronto, Canada

Competing Interests: none declared

Thank you for your responses to Reviewer One Comments #1-3.

Re: Authors response to Reviewer One, Comment #1

This is in regards to the text: “A view has been expressed that autism is currently underdiagnosed in more intellectually-able females compared with males. We found that 34% of women compared with only 27% of men with autism reported accompanying intellectual disabilities, so the female population with autism was intellectually less able than the male population with autism. Our findings therefore provide some evidence to support the view of under-diagnosis of autism in the more intellectually-able women.”

I am still unable to follow the logic of the interpretation “Our findings therefore provide some evidence to support the view of under-diagnosis of autism in the more intellectually-able women?” Has this something to do with an underlying assumption that the female autism population and the male autism population are the same intellectually? If so is there any clinical evidence for this? Or perhaps to do with the nature of self/proxy reporting and the likelihood that there was proxy (rather than self) reporting for intellectually disabled individuals? Or perhaps to do with whether the interpretation of the result relates to the total population of males with autism and the total population of females with autism or referring only to the population of males with ID and the population with females with ID – or referring to “the more intellectually-able women” within in the population of females with autism and intellectual disability? I wonder if the authors could clarify their logic and assumptions in coming to the conclusion “Our findings therefore provide some evidence to support the view of under-diagnosis of autism in the more intellectually-able women?”.

**\*\*\*Response:** Please see the response to the editor comment 3 above. We have revised this paragraph of the discussion with the addition of doubt through insertion of the word “may”, and the addition of a sentence at the end of the paragraph (page 11): “Our findings may therefore provide some evidence to support the view of under-diagnosis of autism in the more intellectually-able women. Alternatively, women and men with autism may actually be intellectually different”

Re: Authors response to Reviewer One, Comment #2

Reviewer One: Thank you for drawing readers attention to this in the strengths and limitations section.

**\*\*\*\*Response:** Thank you.

Re: Authors response to Reviewer One, Comment #3

Reviewer One: I anticipate many readers would be interested in these related studies (autism in this data set with and without reported intellectual disabilities) and comparison of OR for the variables studied between autism with and without intellectual disabilities. Perhaps this reference(s) could be provided?

**\*\*\*Response:** We now reference the work in the discussion (page 11): “We have previously reported Census findings on comorbidities for people with intellectual disabilities.<sup>15</sup>” One further paper is not referenced as it is currently under review.

### VERSION 3 – REVIEW

REVIEWER	Traolach Brugha
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	University of Leicester, UK
<b>REVIEW RETURNED</b>	12-May-2018

<b>GENERAL COMMENTS</b>	<p>One presumes one householder completed the census form on behalf of all occupants. Please expand the methods to describe how this was done in respect of the health questions. Was there any pilot testing of this aspect?</p> <p>Please consider referring to this in the limitations section.</p> <p>The limitations should make more clear to less well versed readers that the census method used is likely to have underestimated milder forms of autism that are probably under diagnosed in adulthood in whom levels of comorbidity may be lower.</p> <p>Table 1 shows lower rates of census reported autism in older adults. The authors did not comment on this although they did comment on the reduction in comorbidity rates with increasing age as being likely due to reduced survival. Do they wish to comment on this or do they judge this to be beyond the remit of this article?</p>
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### VERSION 3 – AUTHOR RESPONSE

#### Reviewer's Reports:

Reviewer: 1

Reviewer Name: Traolach Brugha

Institution and Country: University of Leicester, UK

Competing Interests: None.

One presumes one householder completed the census form on behalf of all occupants. Please expand the methods to describe how this was done in respect of the health questions. Was there any pilot testing of this aspect?

Please consider referring to this in the limitations section.

\*\*\* Response: There was cognitive question testing of the whole census form, including testing for completion of household visitors as well as usual residents, but given the large number of households included in the Census, it is not possible to state exactly how each household completed it. We have added the Census term 'household reference person' to this part of the methods, so that the information is more prominent (page 6):

'One householder on behalf of all occupants in private households (the household reference person), and manager on behalf of all occupants in communal dwellings, was required to complete the Census information. The Census team also followed up non-responders and provided help to respond when needed.'

We have also added this as a further limitation to the discussion (page 12):

'Given the large number of households, we are unable to state how each household reference person approached completing the Census form, although cognitive question testing was completed with a broad range of 70 respondents on the whole questionnaire in advance of the Census (in addition to the 102 respondents who completed cognitive question testing interviews specifically on the health questions).'

The limitations should make more clear to less well versed readers that the census method used is likely to have underestimated milder forms of autism that are probably under diagnosed in adulthood in whom levels of comorbidity may be lower.

\*\*\* Response: We agree with the reviewer. In the 'Strengths and Limitations' section of the discussion where we discuss the prevalence rate of autism and the narrower definition of autism used in the past, we have added the following limitation (page 12):

'It is important to note that undiagnosed adults with milder forms of autism may have lower levels of comorbidity than those with more severe autism.'

Table 1 shows lower rates of census reported autism in older adults. The authors did not comment on this although they did comment on the reduction in comorbidity rates with increasing age as being likely due to reduced survival. Do they wish to comment on this or do they judge this to be beyond the remit of this article?

\*\*\*Response: We were able to state with some certainty that people with intellectual disabilities die earlier than other people, in view of several studies on the topic and a recent systematic review. There is some evidence to suggest this may also be the case for people with autism, but this has been much less studied; hence we have drawn attention to this finding in the results section (page 9), but been cautious in our interpretation of it by stating the following:

'The rate of autism was lowest in the oldest age groups (autism may be associated with reduced life expectancy).'